10/629,749

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	123	(anhydroecgonine or methylecgonidine or anhydromethylecgonine)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:17
L2	2	l1 same antibod?	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:23
L3	208	(anhydroecgonine or methylecgonidine or anhydromethylecgonine or ecgonidine)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:22
L4	17	l3 and antibod?	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:23
L5	20	l3 and antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:24
L6	2	l1 same antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:23
L7	98	crack adj cocaine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:42
L8	48	l7 same antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:24

EAST Search History

L9	7	l8 and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 14:25
L10	11	l7 and immunoassay$1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:05
L11	235	cocaine adj metabolite$1	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:05
L12	165	l11 and antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:06
L13	73	l11 same antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:06
L14	2	anhydroecgonine same antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:19
L15	2	ecgonidine same antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:18
L16	1	ecgonidine near3 antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:19

EAST Search History

L17	2	anhydroecgonine near3 antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:19
L18	2	"20020177714"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:25
L19	2	"20050026303"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 15:27
L20	2	("5376667").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/06/06 16:00
L21	126	monoclonal adj antibod$3 same cocaine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:01
L22	2	l21 and (ecgonidine or methylecgonidine or anhydroecgonine)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:04
L23	109	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) and (immunogen or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:16
L24	0	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) same (immunogen or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:06

EAST Search History

L25	0	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) near5 (immunogen or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:07
L26	9	l23 and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:07
L27	112	(ecgonidine or methylecgonidine or anhydroecgonine or anhydromethylecgonine) and (immunogen or conjugate or hapten or carrier or BSA or KHL or albumin or globulin)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:16
L28	9	l27 and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:31
L29	2	("5821249").PN.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2006/06/06 16:17
L30	1	natalie near1 lu and monoclonal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:32
L31	1	natalie near1 lu and cocaine	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:33
L32	1	(anhydroecgonine and ecgonidine and monoclonal and immunogen and carrier and BSA and KLH and ovalbumin and albumin).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:35

EAST Search History

L33	1	(anhydroecgonine and ecgonidine and monoclonal).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/06/06 16:35

10/625,749

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NEWS 11	APR 03	Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL
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NEWS 14	APR 12	Improved structure highlighting in FQHIT and QHIT display in MARPAT
NEWS 15	APR 12	Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected
NEWS 16	MAY 10	CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 17	MAY 11	KOREAPAT updates resume
NEWS 18	MAY 19	Derwent World Patents Index to be reloaded and enhanced
NEWS 19	MAY 30	IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 20	MAY 30	The F-Term thesaurus is now available in CA/CAplus
NEWS 21	JUN 02	The first reclassification of IPC codes now complete in INPADOC

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```
=> s (anhydroecgonine or ecgonidine or methylecgonidine or andydromethylecgonine)
           144 ANHYDROECGONINE
             2 ANHYDROECGONINES
           144 ANHYDROECGONINE
                 (ANHYDROECGONINE OR ANHYDROECGONINES)
            60 ECGONIDINE
            38 METHYLECGONIDINE
             1 METHYLECGONIDINES
            38 METHYLECGONIDINE
                 (METHYLECGONIDINE OR METHYLECGONIDINES)
             0 ANDYDROMETHYLECGONINE
L1         211 (ANHYDROECGONINE OR ECGONIDINE OR METHYLECGONIDINE OR ANDYDROMET
               HYLECGONINE)

=> s l1 and antibod?
        462722 ANTIBOD?
L2           3 L1 AND ANTIBOD?

=> d l2 ibib abs hitstr tot

L2   ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:99022  CAPLUS
DOCUMENT NUMBER:          142:171445
TITLE:                    Monoclonal antibodies specific for crack
                          cocaine metabolites, a cell line producing the same,
                          and crack cocaine conjugates
INVENTOR(S):              Lu, Natalie T.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 8 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005026303	A1	20050203	US 2003-629749	20030730
PRIORITY APPLN. INFO.:			US 2003-629749	20030730

AB A monoclonal **antibody**, and a cell line capable of producing the same, has been produced with the ability to detect the primary metabolites generated from the pyrolysis of smokeable, or "crack", cocaine. This monoclonal **antibody**, while being highly specific for **anhydroecgonine** Me ester (AEME) and **ecgonidine** (ECD), does not cross-react at a significant level with the primary cocaine metabolites of powdered or injected cocaine. Crack cocaine metabolite-protein conjugates with or without linkers are used to immunize animals for the production of monoclonal **antibodies**. The **antibodies** can be used in immunoassays to discriminate between the use of crack cocaine and the powdered or injected forms.

L2 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2003:957786 CAPLUS
DOCUMENT NUMBER:	140:138736
TITLE:	Three-Dimensional Quantitative Structure-Activity Relationship Modeling of Cocaine Binding by a Novel Human Monoclonal **Antibody**
AUTHOR(S):	Paula, Stefan; Tabet, Michael R.; Farr, Carol D.; Norman, Andrew B.; Ball, W. James, Jr.
CORPORATE SOURCE:	College of Medicine, Department of Pharmacology and Cell Biophysics, University of Cincinnati, Cincinnati, OH, 45267-0575, USA
SOURCE:	Journal of Medicinal Chemistry (2004), 47(1), 133-142 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER:	American Chemical Society
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Human monoclonal **antibodies** (mAbs) designed for immunotherapy have a high potential for avoiding the complications that may result from human immune system responses to the introduction of nonhuman mAbs into patients. This study presents a characterization of cocaine/ **antibody** interactions that determine the binding properties of the novel human sequence mAb 2E2 using three-dimensional quant. structure-activity relationship (3D-QSAR) methodol. We have exptl. determined the binding affinities of mAb 2E2 for cocaine and 38 cocaine analogs. The Kd of mAb 2E2 for cocaine was 4 nM, indicating a high affinity. Also, mAb 2E2 displayed good cocaine specificity, as reflected in its 10-, 1500-, and 25000-fold lower binding affinities for the three physiol. relevant cocaine metabolites benzoylecgonine, ecgonine Me ester, and ecgonine, resp. 3D-QSAR models of cocaine binding were developed by comparative mol. similarity index anal. (CoMSIA). A model of high statistical quality was generated showing that cocaine binds to mAb 2E2 in a sterically restricted binding site that leaves the Me group attached to the ring nitrogen of cocaine solvent-exposed. The Me ester group of cocaine appears to engage in attractive van der Waals interactions with mAb 2E2, whereas the Ph group contributes to the binding primarily via hydrophobic interactions. The model further indicated that an increase in partial pos. charge near the nitrogen proton and Me ester carbonyl group enhances binding affinity and that the ester oxygen likely forms an intermol. hydrogen bond with mAb 2E2. Overall, the cocaine binding properties of mAb 2E2 support its clin. potential for development as a treatment of cocaine overdose and addiction.

REFERENCE COUNT:	40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2002:182723 CAPLUS
DOCUMENT NUMBER:	136:386282

TITLE: Synthesis, Properties, and Reactivity of Cocaine Benzoylthio Ester Possessing the Cocaine Absolute Configuration
AUTHOR(S): Isomura, Shigeki; Hoffman, Timothy Z.; Wirsching, Peter; Janda, Kim D.
CORPORATE SOURCE: Department of Chemistry BCC-582, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (2002), 124(14), 3661-3668
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:386282

AB One aspect of immunopharmacotherapy for cocaine abuse involves the use of a catalytic monoclonal **antibody** (mAb) to degrade cocaine via hydrolysis of the benzoate ester. A cocaine benzoylthio ester analog provides a means to implement high-throughput selection strategies to potentially isolate mAbs with high activity. The required analog was synthesized starting from (-)-cocaine hydrochloride and possessed the cocaine absolute configuration. Key points in the preparation were the introduction of the sulfur atom at C-3 via a bromomagnesium thiolate addition to the exo face of **anhydroecgonine**, separation of C-2 diastereomers, recycling of a C-2 thio ester byproduct, and formation of the necessary C-2 Me and C-3 benzoylthio esters. Effects resulting from the lower electronegativity and greater hydrophobicity of sulfur compared to oxygen were observed These characteristics could result in interesting drug properties. Furthermore, the analog was found to be a substrate for catalytic mAbs that hydrolyze cocaine as monitored by HPLC and also spectrophotometry by coupling cleavage of the benzoylthio ester to the disulfide exchange with Ellman's reagent. Screening **antibody** libraries with the new cocaine analog using the spectroscopic assay provides an avenue for the high-throughput identification of catalysts that efficiently breakdown cocaine.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
=> s crack cocaine
        108011 CRACK
         59042 CRACKS
        142529 CRACK
                  (CRACK OR CRACKS)
         19976 COCAINE
            45 COCAINES
         19981 COCAINE
                  (COCAINE OR COCAINES)
L3          67 CRACK COCAINE
                  (CRACK(W)COCAINE)

=> s l3 and antibod?
        462722 ANTIBOD?
L4           3 L3 AND ANTIBOD?

=> s l4 not l2
L5           2 L4 NOT L2

=> d l5 ibib abs hitstr tot

L5   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:       2005:391023  CAPLUS
TITLE:                  Risk factors for Kaposi's sarcoma among HHV-8
                        seropositive homosexual men with AIDS
AUTHOR(S):              Nawar, Eric; Mbulaiteye, Sam M.; Gallant, Joel E.;
                        Wohl, David A.; Ardini, Marianne; Hendershot, Tabitha;
```

Goedert, James J.; Rabkin, Charles S.
CORPORATE SOURCE: The AIDS Cancer Cohort ACC Study Collaborators, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Department of Health and Human Services, National Institutes of Health, Bethesda, MD, USA
SOURCE: International Journal of Cancer (2005), 115(2), 296-300
CODEN: IJCNAW; ISSN: 0020-7136
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Kaposi's sarcoma (KS) is a frequent complication of the acquired immunodeficiency syndrome (AIDS) in homosexual men. Risk factors for developing this malignancy are uncertain, other than immunosuppression and coinfection with human herpesvirus 8 (HHV-8). We therefore examined factors associated with KS in a cross-sectional anal. of 99 cases among 503 HHV-8 seropos. homosexual men with AIDS. Data were collected by computer-assisted personal interviews and medical chart reviews. HHV-8 seroreactivity was determined by ELISA for **antibodies** against HHV-8 K8.1 glycoprotein. KS was significantly less common in blacks compared to whites [risk ratio (RR) = 0.4; 95% CI = 0.2=0.8] and more common in subjects who had completed college (RR = 1.7; 95% CI = 1.1-2.7) or had annual income greater than $30,000 (RR = 1.5; 95% CI = 1.1-2.2). KS was less common in cigarette smokers (RR = 0.6; 95% CI = 0.5-0.9) and users of **crack cocaine** (RR = 0.4; 95% CI = 0.1-0.8). KS was less common in bisexual men compared to men who were exclusively homosexual (estimated RR = 0.6; 95% CI = 0.4-0.9) and inversely associated with number of female partners. KS was also less common in men who had received pay for sex (RR = 0.6; 95% CI = 0.4-1.0). These cross-sectional assocns. could be biased by potential differences in relative timing of HHV-8 and HIV infection, a postulated determinant of KS risk. Alternatively, our findings may reflect factors protective against KS in individuals infected with HHV-8. Future research should focus on identifying practical measures for countering KS that do not increase the risk of other diseases.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:237608 CAPLUS
DOCUMENT NUMBER: 126:259082
TITLE: Acute activation of circulating polymorphonuclear neutrophils following in vivo administration of cocaine. A potential etiology for pulmonary injury
AUTHOR(S): Baldwin, Gayle Cocita; Buckley, Dawn M.; Roth, Michael D.; Kleerup, Eric C.; Tashkin, Donald P.
CORPORATE SOURCE: Divisions of Hematology-Oncology and Pulmonary and Critical Care, Department of Medicine, UCLA School of Medicine, Los Angeles, CA, 90095-1678, USA
SOURCE: Chest (1997), 111(3), 698-705
CODEN: CHETBF; ISSN: 0012-3692
PUBLISHER: American College of Chest Physicians
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Crack cocaine** has become a major drug of abuse in the United States and its use is associated with a broad spectrum of pulmonary complications. The present study was conducted to determine whether controlled in vivo administration of cocaine (inhaled or IV) alters the function of circulating inflammatory cells in a manner capable of contributing to acute lung injury. Subjects who regularly smoked **crack cocaine** were asked to abstain from illicit drug use for at least 8 h, and were then administered one of the following treatments on each of 4 study days: inhaled cocaine base (45 mg), inhaled placebo (4.5 mg cocaine base, a subphysiol. dose), IV cocaine HCl (0.35 to 0.50 mg/kg), or IV

placebo (saline solution). Samples of blood were obtained from a peripheral venous catheter and blood cells were isolated before and 10 to 45 min after treatment. The administration of either cocaine base or cocaine HCl, but not their corresponding placebos, resulted in the activation of circulating polymorphonuclear neutrophils (PMNs). Exposure to cocaine in vivo enhanced the antibacterial activity of PMNs, as measured by their ability to kill Staphylococcus aureus. Antitumor activity, as measured in an **antibody**-dependent cell-mediated cytotoxicity assay, also increased following short-term administration of cocaine. Finally, short-term exposure to cocaine enhanced production of interleukin 8, a potent PMN chemoattractant and neutrophil-activating factor associated with both acute and chronic lung injury. These studies demonstrate that short-term in vivo exposure to cocaine activates the effector function and cytokine production of circulating PMNs. Therefore, it is possible that bursts of acute inflammatory activity resulting from crack use could contribute to lung injury.

```
=> s (anhydroecgonine or ecgonidine or methylecgonidine or andydromethylecgonine or
crack cocaine)
           144 ANHYDROECGONINE
             2 ANHYDROECGONINES
           144 ANHYDROECGONINE
                 (ANHYDROECGONINE OR ANHYDROECGONINES)
            60 ECGONIDINE
            38 METHYLECGONIDINE
             1 METHYLECGONIDINES
            38 METHYLECGONIDINE
                 (METHYLECGONIDINE OR METHYLECGONIDINES)
             0 ANDYDROMETHYLECGONINE
        108011 CRACK
         59042 CRACKS
        142529 CRACK
                 (CRACK OR CRACKS)
         19976 COCAINE
            45 COCAINES
         19981 COCAINE
                 (COCAINE OR COCAINES)
            67 CRACK COCAINE
                 (CRACK(W)COCAINE)
L6         264 (ANHYDROECGONINE OR ECGONIDINE OR METHYLECGONIDINE OR ANDYDROMET
               HYLECGONINE OR CRACK COCAINE)

=> s l6 and immunoassy?
            31 IMMUNOASSY?
L7           0 L6 AND IMMUNOASSY?

=> s l6 and monoclonal
        139709 MONOCLONAL
           525 MONOCLONALS
        139770 MONOCLONAL
                 (MONOCLONAL OR MONOCLONALS)
L8           3 L6 AND MONOCLONAL

=> s l8 not l5 l2
MISSING OPERATOR L5 L2
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l8 not l5
L9           3 L8 NOT L5

=> s l9 not l2
L10          0 L9 NOT L2
```

```
=> cocaine and monoclonal
COCAINE IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s cocaine and monoclonal
         19976 COCAINE
            45 COCAINES
         19981 COCAINE
                 (COCAINE OR COCAINES)
        139709 MONOCLONAL
           525 MONOCLONALS
        139770 MONOCLONAL
                 (MONOCLONAL OR MONOCLONALS)
L11        134 COCAINE AND MONOCLONAL

=> s l11 and (AEME or ECD or ecgonidine or anhydroecgonine or methylecgonidine or
anhydromethylecgonine)
            26 AEME
          4705 ECD
           142 ECDS
          4766 ECD
                 (ECD OR ECDS)
            60 ECGONIDINE
           144 ANHYDROECGONINE
             2 ANHYDROECGONINES
           144 ANHYDROECGONINE
                 (ANHYDROECGONINE OR ANHYDROECGONINES)
            38 METHYLECGONIDINE
             1 METHYLECGONIDINES
            38 METHYLECGONIDINE
                 (METHYLECGONIDINE OR METHYLECGONIDINES)
             0 ANHYDROMETHYLECGONINE
L12          3 L11 AND (AEME OR ECD OR ECGONIDINE OR ANHYDROECGONINE OR METHYLE
               CGONIDINE OR ANHYDROMETHYLECGONINE)

=> s l12 not l2
L13          0 L12 NOT L2

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                               77.98      78.19

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                               -3.75      -3.75

STN INTERNATIONAL LOGOFF AT 15:15:21 ON 06 JUN 2006
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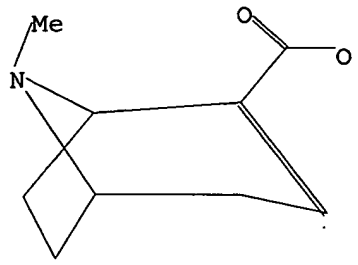
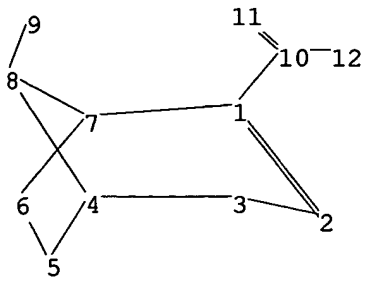


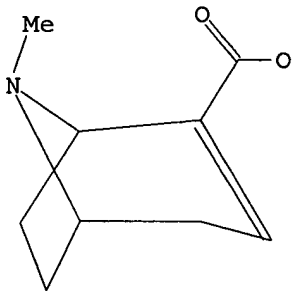


chain nodes :
9 10 11 12
ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
1-10 8-9 10-11 10-12
ring bonds :
1-2 1-7 2-3 3-4 4-5 4-8 5-6 6-7 7-8
exact/norm bonds :
1-2 1-7 2-3 3-4 4-8 7-8 10-11 10-12
exact bonds :
1-10 4-5 5-6 6-7 8-9
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS 11:CLASS 12:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 08:04:23 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 263 TO ITERATE

100.0% PROCESSED 263 ITERATIONS 8 ANSWERS
SEARCH TIME: 00.00.01

```
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          4287 TO     6233
PROJECTED ANSWERS:                8 TO      329

L2             8 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 08:04:31 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     4919 TO ITERATE

100.0% PROCESSED     4919 ITERATIONS                          160 ANSWERS
SEARCH TIME: 00.00.01

L3           160 SEA SSS FUL L1

=> FIL CAPLUS
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                 166.94     167.15

FILE 'CAPLUS' ENTERED AT 08:04:37 ON 07 JUN 2006
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FILE LAST UPDATED: 6 Jun 2006  (20060606/ED)

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=> s l3
L4           266 L3

=> s l3 and antibod?
             266 L3
          462814 ANTIBOD?
L5             6 L3 AND ANTIBOD?

=> s l3 and monoclonal
             266 L3
          139728 MONOCLONAL
             525 MONOCLONALS
          139789 MONOCLONAL
                 (MONOCLONAL OR MONOCLONALS)
L6             4 L3 AND MONOCLONAL

=> s l4 and monoclonal
          139728 MONOCLONAL
```
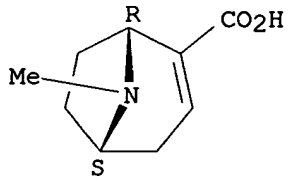

```
          525 MONOCLONALS
       139789 MONOCLONAL
                (MONOCLONAL OR MONOCLONALS)
L7           4 L4 AND MONOCLONAL

=> dup rem l5 l7
PROCESSING COMPLETED FOR L5
PROCESSING COMPLETED FOR L7
L8           6 DUP REM L5 L7 (4 DUPLICATES REMOVED)
               ANSWERS '1-6' FROM FILE CAPLUS

=> s l4 and (immunogen or hapten or conjugate)
          6256 IMMUNOGEN
          3508 IMMUNOGENS
          8742 IMMUNOGEN
                (IMMUNOGEN OR IMMUNOGENS)
          9760 HAPTEN
          6712 HAPTENS
         12327 HAPTEN
                (HAPTEN OR HAPTENS)
         64873 CONJUGATE
         57977 CONJUGATES
        100624 CONJUGATE
                (CONJUGATE OR CONJUGATES)
L9          14 L4 AND (IMMUNOGEN OR HAPTEN OR CONJUGATE)

=> s l9 not l8
L10          6 S L8
L11         11 L9 NOT L10

=> d l8 ibib abs hitstr tot

L8   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2006 ACS on STN  DUPLICATE 1
ACCESSION NUMBER:         2005:99022  CAPLUS
DOCUMENT NUMBER:          142:171445
TITLE:                    Monoclonal antibodies specific for crack
                          cocaine metabolites, a cell line producing the same,
                          and crack cocaine conjugates
INVENTOR(S):              Lu, Natalie T.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 8 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2005026303         A1    20050203    US 2003-629749          20030730
PRIORITY APPLN. INFO.:                       US 2003-629749          20030730
AB   A monoclonal antibody, and a cell line capable of producing the
     same, has been produced with the ability to detect the primary metabolites
     generated from the pyrolysis of smokeable, or "crack", cocaine.  This
     monoclonal antibody, while being highly specific for
     anhydroecgonine Me ester (AEME) and ecgonidine (ECD), does not cross-react
     at a significant level with the primary cocaine metabolites of powdered or
     injected cocaine.  Crack cocaine metabolite-protein conjugates with or
     without linkers are used to immunize animals for the production of monoclonal
     antibodies.  The antibodies can be used in immunoassays
     to discriminate between the use of crack cocaine and the powdered or injected
     forms.
IT   484-93-5, Ecgonidine 43021-26-7, Anhydroecgonine methyl
```

Applicant

ester
RL: ANT (Analyte); ANST (Analytical study)
(monoclonal **antibodies** specific for crack cocaine metabolites for use in immunoassays)

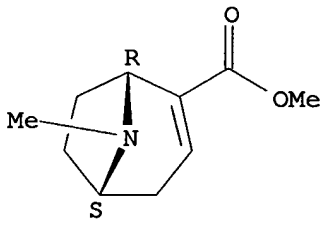
RN 484-93-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 43021-26-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

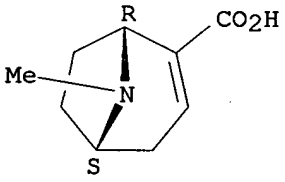
Absolute stereochemistry. Rotation (-).



IT **484-93-5D**, Ecgonidine, protein conjugates **43021-26-7D**, Anhydroecgonine methyl ester, protein conjugates
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(monoclonal **antibodies** specific for crack cocaine metabolites for use in immunoassays)

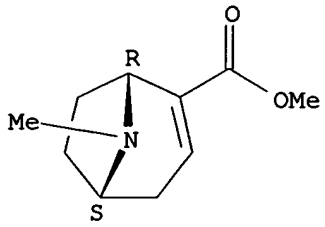
RN 484-93-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 43021-26-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



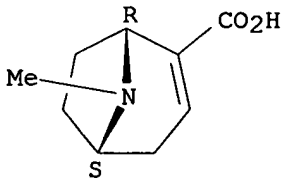
L8 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:957786 CAPLUS
DOCUMENT NUMBER: 140:138736
TITLE: Three-Dimensional Quantitative Structure-Activity Relationship Modeling of Cocaine Binding by a Novel Human Monoclonal **Antibody**
AUTHOR(S): Paula, Stefan; Tabet, Michael R.; Farr, Carol D.; Norman, Andrew B.; Ball, W. James, Jr.
CORPORATE SOURCE: College of Medicine, Department of Pharmacology and Cell Biophysics, University of Cincinnati, Cincinnati, OH, 45267-0575, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(1), 133-142
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Human monoclonal **antibodies** (mAbs) designed for immunotherapy have a high potential for avoiding the complications that may result from human immune system responses to the introduction of nonhuman mAbs into patients. This study presents a characterization of cocaine/**antibody** interactions that determine the binding properties of the novel human sequence mAb 2E2 using three-dimensional quant. structure-activity relationship (3D-QSAR) methodol. We have exptl. determined the binding affinities of mAb 2E2 for cocaine and 38 cocaine analogs. The Kd of mAb 2E2 for cocaine was 4 nM, indicating a high affinity. Also, mAb 2E2 displayed good cocaine specificity, as reflected in its 10-, 1500-, and 25000-fold lower binding affinities for the three physiol. relevant cocaine metabolites benzoylecgonine, ecgonine Me ester, and ecgonine, resp. 3D-QSAR models of cocaine binding were developed by comparative mol. similarity index anal. (CoMSIA). A model of high statistical quality was generated showing that cocaine binds to mAb 2E2 in a sterically restricted binding site that leaves the Me group attached to the ring nitrogen of cocaine solvent-exposed. The Me ester group of cocaine appears to engage in attractive van der Waals interactions with mAb 2E2, whereas the Ph group contributes to the binding primarily via hydrophobic interactions. The model further indicated that an increase in partial pos. charge near the nitrogen proton and Me ester carbonyl group enhances binding affinity and that the ester oxygen likely forms an intermol. hydrogen bond with mAb 2E2. Overall, the cocaine binding properties of mAb 2E2 support its clin. potential for development as a treatment of cocaine overdose and addiction.

IT **484-93-5**, Ecgonidine
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(three-dimensional quant. structure-activity relationship modeling of cocaine binding by a novel human monoclonal **antibody**)

RN 484-93-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

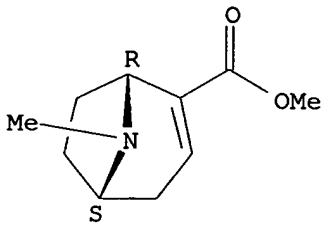
ACCESSION NUMBER: 2002:182723 CAPLUS
DOCUMENT NUMBER: 136:386282
TITLE: Synthesis, Properties, and Reactivity of Cocaine Benzoylthio Ester Possessing the Cocaine Absolute Configuration
AUTHOR(S): Isomura, Shigeki; Hoffman, Timothy Z.; Wirsching, Peter; Janda, Kim D.
CORPORATE SOURCE: Department of Chemistry BCC-582, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Journal of the American Chemical Society (2002), 124(14), 3661-3668
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:386282

AB One aspect of immunopharmacotherapy for cocaine abuse involves the use of a catalytic monoclonal **antibody** (mAb) to degrade cocaine via hydrolysis of the benzoate ester. A cocaine benzoylthio ester analog provides a means to implement high-throughput selection strategies to potentially isolate mAbs with high activity. The required analog was synthesized starting from (-)-cocaine hydrochloride and possessed the cocaine absolute configuration. Key points in the preparation were the introduction of the sulfur atom at C-3 via a bromomagnesium thiolate addition to the exo face of anhydroecgonine, separation of C-2 diastereomers, recycling of a C-2 thio ester byproduct, and formation of the necessary C-2 Me and C-3 benzoylthio esters. Effects resulting from the lower electronegativity and greater hydrophobicity of sulfur compared to oxygen were observed These characteristics could result in interesting drug properties. Furthermore, the analog was found to be a substrate for catalytic mAbs that hydrolyze cocaine as monitored by HPLC and also spectrophotometry by coupling cleavage of the benzoylthio ester to the disulfide exchange with Ellman's reagent. Screening **antibody** libraries with the new cocaine analog using the spectroscopic assay provides an avenue for the high-throughput identification of catalysts that efficiently breakdown cocaine.

IT **43021-26-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of a cocaine benzoylthio ester analog possessing the cocaine absolute configuration and evaluation of it as a substrate for cocaine hydrolyzing catalytic monoclonal **antibodies**)

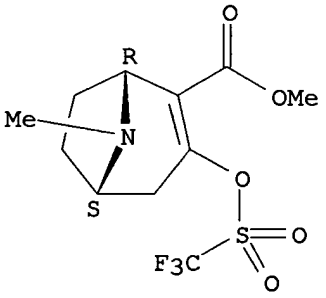
RN 43021-26-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



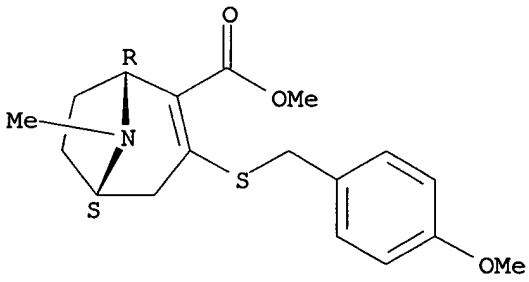
IT **168143-65-5P 426813-48-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of a cocaine benzoylthio ester analog possessing the cocaine absolute configuration and evaluation of it as a substrate for cocaine hydrolyzing catalytic monoclonal **antibodies**)
RN 168143-65-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



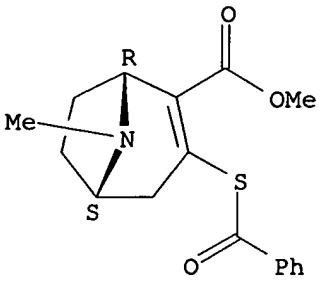
RN 426813-48-1 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-[[(4-methoxyphenyl)methyl]thio]-8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



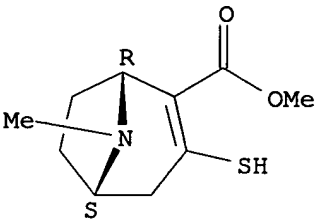
IT **426813-47-0P 426813-50-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of a cocaine benzoylthio ester analog possessing the cocaine absolute configuration and evaluation of it as a substrate for cocaine hydrolyzing catalytic monoclonal **antibodies**)
RN 426813-47-0 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-(benzoylthio)-8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 426813-50-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-mercapto-8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



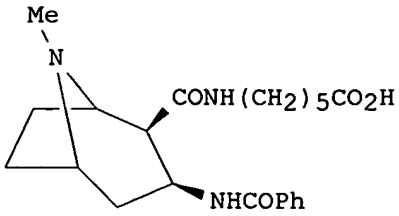
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1997:516313 CAPLUS
DOCUMENT NUMBER: 127:121907
TITLE: Preparation of cocaine derivatives as an anti-cocaine vaccine
INVENTOR(S): Wirsching, Peter; Janda, Kim D.
PATENT ASSIGNEE(S): Scripps Research Institute, USA; Wirsching, Peter; Janda, Kim D.
SOURCE: PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9721451	A1	19970619	WO 1996-US19982		19961216
W: AU, CA, US					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2239058	AA	19970619	CA 1996-2239058		19961216
AU 9715658	A1	19970703	AU 1997-15658		19961216
AU 719289	B2	20000504			
EP 967993	A2	20000105	EP 1996-945392		19961216
R: DE, FR, GB, IT, NL					
US 6383490	B1	20020507	US 1998-77434		19980612
PRIORITY APPLN. INFO.:			US 1995-572849	A2	19951214
			WO 1996-US19982	W	19961216

OTHER SOURCE(S): MARPAT 127:121907

GI



I

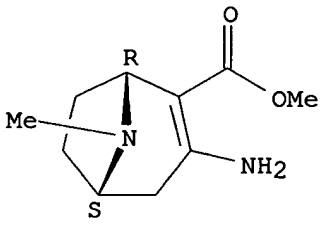
AB Cocaine analogs, e.g. I, and their protein conjugates, are prepared for use as anticocaine vaccines. An anti-cocaine vaccine employs a cocaine hapten conjugated to a carrier protein. The anti-cocaine vaccine elicits an immune response which reduces the psychoactive effects of cocaine consumption by the production of anticocaine polyclonal **antibodies**. The **antibodies** may be employed in an ELISA test for assaying cocaine. The immune response elicited by the anti-cocaine vaccine produces **antibody** producing cells which may be isolated and cloned for producing anti-cocaine monoclonal **antibodies**.

IT **180633-51-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of cocaine derivs. as an anticocaine vaccine)

RN 180633-51-6 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-amino-8-methyl-, methyl ester, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L8 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:75293 CAPLUS

DOCUMENT NUMBER: 141:3203

TITLE: Substrate-assisted **antibody** catalysis

AUTHOR(S): Deng, Shixian; Bharat, Narine; de Prada, Paloma; Landry, Donald W.

CORPORATE SOURCE: Department of Medicine, Division of Clinical Pharmacology and Experimental Therapeutics, Columbia University, New York, NY, 10032, USA

SOURCE: Organic & Biomolecular Chemistry (2004), 2(3), 288-290
CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:3203

AB A new strategy in transition-state analog design is demonstrated to elicit catalytic **antibodies**. The strategy is based on substrate-assisted **antibody** catalysis and utilizes analogs designed to mimic the transition-state for intramol. catalysis and thereby favor **antibodies** that can recruit catalytic groups from

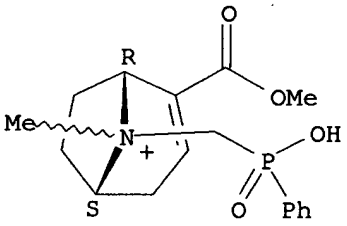
substrate. The hydrolysis of the benzoyl ester of cocaine provides an illustration. The benzoyl ester of cocaine is distant from the protonated nitrogen in the stable chair conformer but proximate in the strained boat form. An **antibody** stabilizing the boat form and approximating ester and amine could catalyze ester hydrolysis. To mimic the transition-state for the intramol. catalysis, we synthesized a cocaine analog that replaces this ester with a methylenephenylphosphinate bridge to the tropane nitrogen. This bridged analog elicited 85 cocaine esterases out of 450 anti-analog **antibodies**-a performance markedly superior to that of a simple phosphonate ester-based analog with an identical tether. The correspondence of the analog to a "high energy" conformer eliminated product inhibition. For certain polyfunctional targets, substrate assistance can be an effective strategy for eliciting catalytic **antibodies**.

IT **697291-39-7**
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative) (decomposition product; design of a transition state analog that elicits cocaine hydrolyzing **antibodies** as an example of substrate-assisted **antibody** catalysis)

RN 697291-39-7 CAPLUS

CN 8-Azoniabicyclo[3.2.1]oct-2-ene, 8-[(hydroxyphenylphosphinyl)methyl]-2-(methoxycarbonyl)-8-methyl-, iodide, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● I^-

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1981:580646 CAPLUS

DOCUMENT NUMBER: 95:180646

TITLE: Cocaine radioimmunossay - structure versus reactivity

AUTHOR(S): Budd, Robert D.

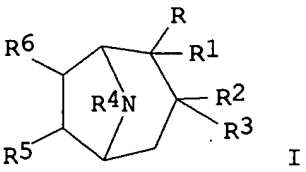
CORPORATE SOURCE: Los Angeles County Med. Examiner-Coroner, Los Angeles, CA, 90033, USA

SOURCE: Clinical Toxicology (1981), 18(7), 773-82
CODEN: CTOXAO; ISSN: 0009-9309

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

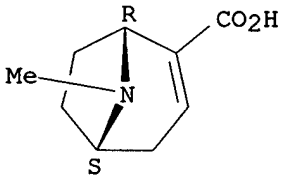
AB Cocaine [50-36-2] and 26 related compds. I (R and R1 = H, CO2H, CO2Me, etc.; R2 = H, OH, OBz; R3 = H, OH, OMe, aralkanoate, etc.; R4 = H, Me; R5 = H, OH, etc.; R6 = H, OH, etc.) were tested for Roche radioimmunoassay (RIA) benzoylecgonine **antibody**-binding activity. Benzoylecgonine [519-09-5] had the optimum **antibody**-binding activity; changes of any of the substituents (excepting esterification of the carboxylic acid group) reduced the binding. Cocaethylene (I; R = CO2Et, R1 = R3 = R5 = R6 = H, R2 = OBz, R4 = Me) [529-38-4] was the only drug which interfered with the Roche RIA of cocaine and its metabolites at therapeutic or overdose levels, but it is seldom encountered in therapeutic use or abuse. Thus, the Roche RIA studied is suitable for the anal. of urine samples for cocaine and its metabolites.

IT **484-93-5**
RL: PROC (Process)
(radioimmunoassay of, structure in relation to)

RN 484-93-5 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:528117 CAPLUS

DOCUMENT NUMBER: 144:150506

TITLE: Development of polyfluorophenyltropanes: Potential probes for 19F magnetic resonance imaging (MRI) and spectroscopy (MRS) assessments of the dopamine transporter

AUTHOR(S): Zhang, Ao; Kula, Nora S.; Zhang, Kehong; Baldessarini, Ross J.; Kaufman, Marc J.; Renshaw, Perry F.; Neumeyer, John L.

CORPORATE SOURCE: Medicinal Chemistry Laboratory, Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, Belmont, MA, 02478-9106, USA

SOURCE: Letters in Drug Design & Discovery (2005), 2(4), 302-306
CODEN: LDDDAW; ISSN: 1570-1808

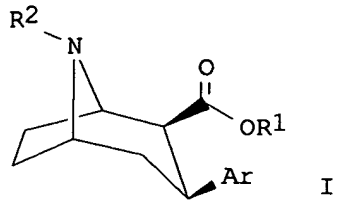
PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:150506

GI



I

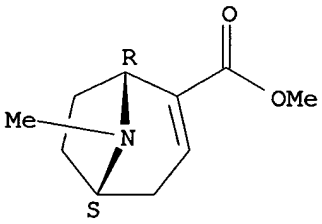
AB A novel series of nonradiolabeled, polyfluorinated phenyltropanes, e.g. I [Ar = Ph, C6H4CF3-4, C6H3(CF3)2-3,5, C6H4(C6H4CF3-4)-4, R1 = R2 = Me; Ar = C6H3(CF3)2-3,5, R1 = Me, R2 = H, (CH2)3F; Ar = C6H4I-4, R1 = CH2CF3, R2 = Me], were developed containing three or more 19F atoms/mol. in a magnetic resonance (MR) equivalent chemical environment to increase coherent MR signal characteristics. Competitive radioreceptor affinity assays of such compds. yielded nM affinity at dopamine (DAT) and serotonin (SERT) transporters in rat brain tissue. Compound I [Ar = C6H4CF3-4, R1 = R2 = Me; (MCL-314)] at 50 μM gave a clear magnetic resonance spectroscopy signal, and I [Ar = C6H4I-4, R1 = CH2CF3, R2 = Me; (MCL-319)] yielded very high DAT potency and improved selectivity over SERT. Such compds. might potentially serve as MRI- or MRS-detectable index ligands for the dopamine transporter proteins, and preliminary observations call for further study of addnl. polyfluorinated phenyltropanes.

IT **43021-26-7P**, Anhydroecgonine methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and stereoselective **conjugate** addition to, by polyfluorinated aryl Grignards; development of polyfluorophenyltropanes as potential probes for 19F magnetic resonance imaging and spectroscopy)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:997722 CAPLUS

DOCUMENT NUMBER: 142:280328

TITLE: Ab initio mo calculation studies for several novel entries to tropane compounds

AUTHOR(S): Forsythe, Kelsey M.; Robertson, Daniel H.; Zheng, Qi-Huang

CORPORATE SOURCE: Department of Chemistry, Indiana University Purdue University at Indianapolis, Indianapolis, IN, 46202, USA

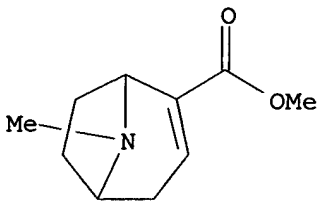
SOURCE: Journal of Theoretical & Computational Chemistry (2004), 3(3), 305-323

CODEN: JTCCAC; ISSN: 0219-6336
PUBLISHER: World Scientific Publishing Co. Pte. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

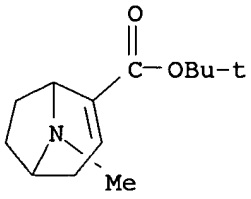
AB Tropane alkaloids are generally known as anticholinergics. Radiolabeled tropane compds. could be brain imaging agents used in biomedical imaging technique positron emission tomog. (PET). A novel entry to aryltropane analogs of cocaine was developed based on the **conjugate** addition reaction of Grignard reagents phenylmagnesium, (4'-isopropenylphenyl)magnesium, or 2-naphthylmagnesium bromide to α,β-unsatd. esters anhydroecgonine Me ester, or t-Bu ester, which gave several aryltropanes with high binding affinities for dopamine and serotonin transporters. Basic conditions are frequently employed in the radiolabeling chemical of many aryltropane cocaine analogs. However, isomerization at C-2 position can also occur under basic conditions, resulting in loss of the biol. potent 2β-isomers by conversion to the much less active 2α-isomer. Tropinone could be envisaged as a convenient starting material for the synthesis of diverse tropane alkaloids. A novel entry into tropane alkaloid intermediates was developed based on the ring-opening reaction of tropinone. In this reaction, the enolate of tropinone, resulting from deprotonation with lithium diisopropylamide [LDA, LiN(CHMe2)2] or sodium bis(trimethylsilyl)amide [NaN(SiMe3)2] was treated with alkyl chloroformate to give a novel, structurally unique class of tropane alkaloid intermediates 6-N-carboalkyoxy-N-methyl-2-cycloheptenone, 1-alkyoxycarboxy-6-N-carboalkoxy-N-methyl-2,7-cyclohept-dien and 6-N-carboalkyoxy-N-methyl-7-carboalkoxy-2,7-cyclohept-dien-ol. In this paper the **conjugate** addition reaction of Grignard reagents to α,β-unsatd. esters, the isomerization of aryltropane cocaine analogs, and the ring-opening reaction of tropinone by ab initio MO calcn. at the Hartree-Fock (HF) level. is studied. The calcn. results solely in terms of energetics indicate that the 2α-isomers (equatorial configurations) of aryltropane cocaine analogs are more stable than their 2β-isomers (axial configurations), at the AM1, STO-3G and 3-21G(*) levels, and the Grignard 1,4- and then 1,2-addition (double addition) products are likely more stable than the Grignard 1,4-addition (single addition) products, at the STO-3G and 3-21G(*) levels except at the AM1 level. Therefore the tendency of Grignard addition toward double addition is competitive with single addition, and the isomerization tends to the formation of more stable 2α-isomers. Likewise, the calcn. results solely in terms of energetics indicate that the stability of the reaction product forms at the AM1, STO-3G and 3-21G(*) levels, and the tendency of alkyl chloroformate addition toward double addition to the products is competitive with single addition to the products. Ab initio MO calcns. provide a theor. rationalization for the chemoselectivity of the **conjugate** addition reaction and the ring-opening reaction, the most stable configurations of reaction products, and the isomerization.

IT **127379-24-2 847487-91-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(ab initio mo calcn. studies for several novel entries to tropane compds. including Grignard **conjugate** addition, isomerization, and ring-opening products)

RN 127379-24-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester (9CI) (CA INDEX NAME)



RN 847487-91-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

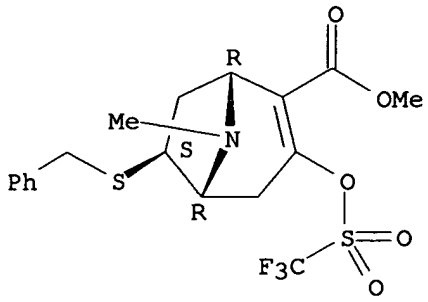
L11 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:956779 CAPLUS
DOCUMENT NUMBER: 142:411512
TITLE: Synthesis of stereoisomers of 6β- and 7β-(benzylthio)-3-(p-tolyl) tropane-2-carboxylic acid methyl ester
AUTHOR(S): Masri, Fadi; Riche, Francoise; Durif, Andre; Philouze, Christian; Vallee, Yannick
CORPORATE SOURCE: Laboratoire d'Etudes Dynamiques et Structurales de la Selectivite, Institut de Chimie Moleculaire de Grenoble, Universite Joseph Fourier Grenoble I, Grenoble, 38041, Fr.
SOURCE: Journal of Sulfur Chemistry (2004), 25(4), 259-268
CODEN: JSCOFC; ISSN: 1741-5993
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:411512

AB To develop new 99mTc-labeled agents to evaluate dopamine transporters (DAT) involved in Parkinson's disease, by in vivo SPECT imaging, we have synthesized six new sulfur-containing ligands with the tropane skeleton. We have introduced the complexing sulfur atom far from the three sites of recognition by DAT of these tropane derivs. The 6β-substituted tropinone has been obtained by a double Mannich condensation followed by the introduction of the moieties for mol. interactions at the binding site on C2 and C3, leading to the six stereoisomers.

IT **848590-43-2P 848590-44-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and palladium-catalyzed coupling of, with tolylboronic acid; synthesis of stereoisomers of 6β- and 7β-(benzylthio)-3-(p-tolyl) tropane-2-carboxylic acid Me ester)

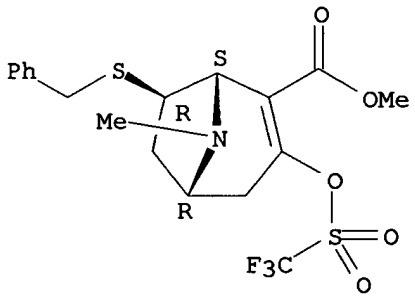
RN 848590-43-2 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-6-[(phenylmethyl)thio]-3-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester, (1R,5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



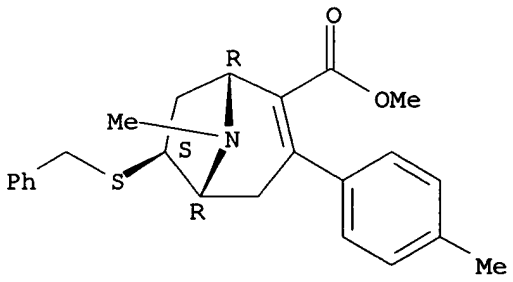
RN 848590-44-3 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-7-[(phenylmethyl)thio]-3-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester, (1R,5S,7S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



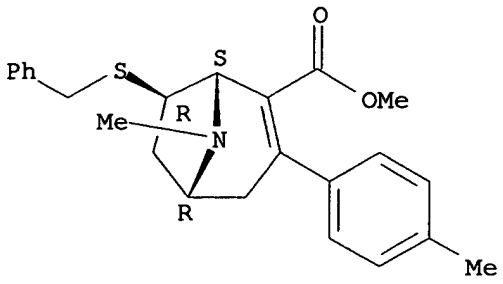
IT **848590-46-5P 848590-47-6P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, crystal structure and **conjugate** reduction of, with samarium iodide; synthesis of stereoisomers of 6β- and 7β-(benzylthio)-3-(p-tolyl) tropane-2-carboxylic acid Me ester)
RN 848590-46-5 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-(4-methylphenyl)-6-[(phenylmethyl)thio]-, methyl ester, (1R,5R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 848590-47-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-(4-methylphenyl)-7-[(phenylmethyl)thio]-, methyl ester, (1R,5S,7S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

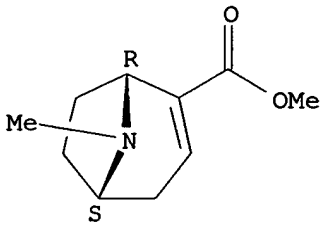
L11 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:344208 CAPLUS
DOCUMENT NUMBER: 141:71743
TITLE: Two- and Three Dimensional Combinatorial Chemistry from Multicomponent Grignard Reagents
AUTHOR(S): Buelow, Anne; Sinning, Steffen; Wiborg, Ove; Bols, Mikael
CORPORATE SOURCE: Department of Chemistry, University of Aarhus, Aarhus, DK-8000, Den.
SOURCE: Journal of Combinatorial Chemistry (2004), 6(4), 509-519
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **conjugate** addition of five component Grignard reagents to Me ecgonidine was used to create libraries of 3-substituted tropanes. By variation in the reagent combination in 10 such 5-membered sublibraries, a library of 25 compds. was made in a two-dimensional format. Screening of this library led to identification of two new potent monoamine transporter ligands that were subsequently synthesized. The most potent compound in this library was (1R,2S,3S,5S)-3-(3,4-dimethylphenyl)-8-methyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid Me ester, which inhibited dopamine transporter (hDAT) binding and reuptake with a Ki of 26 and 20 nM, resp. The **conjugate** addition to a 5-membered library of Me ecgonidine analogs with variation of nitrogen substituent was also carried out and used to create 15 sublibraries of 25 compds., which displayed 125 compds. in a three-dimensional format. From this 3D library, several potent dopamine transport inhibitors were likewise identified and synthesized. The most potent hDAT inhibitor discovered was (1R,2S,3S,5S)-3-(3,4-dimethylphenyl)-8-pentyl-8-azabicyclo[3.2.1]octane-2-carboxylic acid Me ester. The study also showed that 3-alkyltropanes were poor inhibitors of monoamine transporters.

IT **43021-26-7**
RL: CRT (Combinatorial reactant); RCT (Reactant); CMBI (Combinatorial study); RACT (Reactant or reagent)
(preparation of two and three dimensional combinatorial libraries of tropanes via Grignard **conjugate** addition and activity as monoamine transporter inhibitors)

RN 43021-26-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

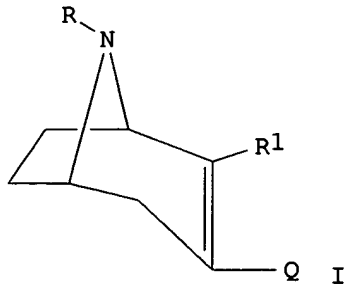


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:416949 CAPLUS
DOCUMENT NUMBER: 135:33571
TITLE: Transition metal-cyclopentadienyl-tropane **conjugates** with affinity for monoamine transporters, their preparation and use as diagnostic or therapeutic agents
INVENTOR(S): Tamagnan, Gilles Denis; Baldwin, Ronald Martin; Innis, Robert B.
PATENT ASSIGNEE(S): Yale University, USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040239	A2	20010607	WO 2000-US42447	20001201
WO 2001040239	A3	20001227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393610	AA	20010607	CA 2000-2393610	20001201
US 2002111486	A1	20020815	US 2000-727076	20001201
EP 1233968	A2	20020828	EP 2000-992372	20001201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003515541	T2	20030507	JP 2001-540994	20001201
PRIORITY APPLN. INFO.:			US 1999-168671P P	19991203
			WO 2000-US42447 W	20001201

OTHER SOURCE(S): MARPAT 135:33571
GI



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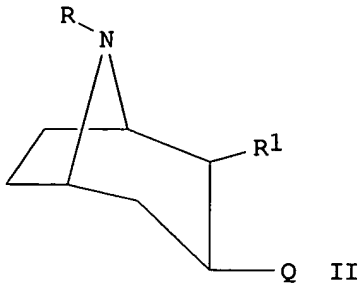
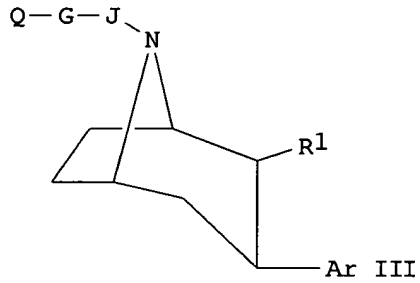


II



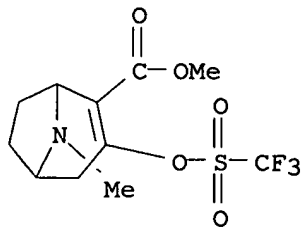
III

AB Transition metal-cyclopentadienyl-tropane **conjugate** compds., e.g., I, II [R1 = CO2R2, CH2OR2; R, R2 = H, (un)branched C1-12 alkyl, C2-12 alkenyl, C2-12 alkynyl, C6-12 aryl, C3-12 cycloalkyl, C3-12 heterocycloalkyl, C1-12 heteroarom. group wherein the heteroatom is N, O or S; Q = (un)substituted CpM(CO)3; M = Re, Tc, Mn or radioisotope; Cp = cyclopentadienyl] or III [Q = (un)substituted CpM(CO)3, same M, Cp; G = direct link, CO, R2NCO, CH:CH, C(O), SO2, O2C, CH2O(CH2)r'O(CH2)s; r = 1-4, s = 0-4, where r + s < 8; J = (CH2)n, n = 1-8; same R1; Ar = (un)substituted Ph group; when R1 = CO2Me or CH2OH, G ≠ CO] useful as radiodiagnostic agents (no data) or as diagnostic or therapeutic agents for treatment of disorders related to monoamine transporter activity, such as clin. diagnosis of Parkinson's disease, are claimed, as are methods for their preparation In an example, the binding affinity Ki of III [R1 = CO2Me, Ar = 4-ClC6H4, J = (CH2)3, G = O2C, Q = CpRe(CO)3; preparation given] for dopamine transporter (DAT) was 4.18 ± 0.33 nM, for serotonin transporter (5-HTT) was 5.28 ± 0.21 nM and for norepinephrine transporter (NET) was 74.0 ± 8.2 nM.

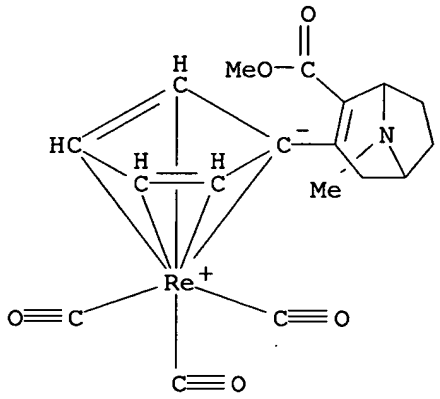
IT **343612-72-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(catalytic coupling reaction of, with [(trimethylstannyl)cyclopentadienyl]rhenium tricarbonyl)

RN 343612-72-6 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-3-[[(trifluoromethyl)sulfonyl]oxy]-, methyl ester (9CI) (CA INDEX NAME)



IT **343612-70-4P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(preparation and binding affinity for dopamine, serotonin and norepinephrine transporters)
RN 343612-70-4 CAPLUS
CN Rhenium, tricarbonyl[(1,2,3,4,5-η)-1-[2-(methoxycarbonyl)-8-methyl-8-azabicyclo[3.2.1]oct-2-en-3-yl]-2,4-cyclopentadien-1-yl]- (9CI) (CA INDEX NAME)



L11 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:512816 CAPLUS
DOCUMENT NUMBER: 129:199620
TITLE: Cocaine Benzoyl Thioester: Synthesis, Kinetics of Base Hydrolysis, and Application to the Assay of Cocaine Esterases
AUTHOR(S): Cashman, John R.; Berkman, Clifford E.; Underiner, Gail; Kolly, Carrie A.; Hunter, Allen D.
CORPORATE SOURCE: Human BioMolecular Research Institute, Seattle, WA, 98199, USA
SOURCE: Chemical Research in Toxicology (1998), 11(8), 895-901
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis and characterization of diastereomers of cocaine benzoyl thioester is described. Allococaine benzoyl thioester and allopseudococaine benzoyl thioester were synthesized by the **conjugate** addition of p-methoxytolyl thiol to ecgonine Me ester followed by debenzylation and benzoylation. The absolute structure of the hydrochloride salt of the major ecgonine p-methoxytolyl sulfide formed was determined by single-crystal diffraction anal. and used to establish the addition geometry. When placed in aqueous solution, the cocaine benzoyl thioester diastereomers hydrolyzed to give thioecgonine Me ester. The rate of cocaine benzoyl thioester hydrolysis was carefully investigated spectrophotometrically by using the Ellman reagent. At neutral pH, the hydrolysis of the diastereomers was found to proceed at detectable rates. Upon increasing pH, the rate of hydrolysis of cocaine benzoyl thioester diastereomers was increased and the reaction was catalyzed by basic buffer species. In addition to defining the kinetics of hydrolysis in aqueous solution, cocaine benzoyl thioester was utilized as a highly efficient method to

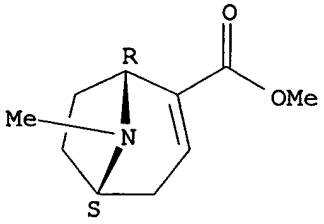
monitor the activity of cholinesterases and pig liver esterase. Use of cocaine benzoyl thioester represents a rapid and sensitive way to screen for cocaine esterase activity.

IT **43021-26-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis, kinetics of base hydrolysis, and application to assay of cocaine esterases of cocaine benzoyl thioester)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:81529 CAPLUS

DOCUMENT NUMBER: 126:171741

TITLE: Stereoselective synthesis of 2β-carbomethoxy-3β-phenyltropane derivatives. Enhanced stereoselectivity observed for the **conjugate** addition reaction of phenylmagnesium bromide derivatives with anhydrous dichloromethane

AUTHOR(S): Xu, Lifen; Trudell, Mark L.

CORPORATE SOURCE: Dep. Chem., Univ. New Orleans, New Orleans, LA, 70148, USA

SOURCE: Journal of Heterocyclic Chemistry (1996), 33(6), 2037-2039
CODEN: JHTCAD; ISSN: 0022-152X

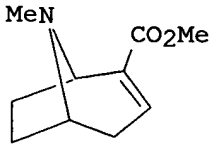
PUBLISHER: HeteroCorporation

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 126:171741

GI



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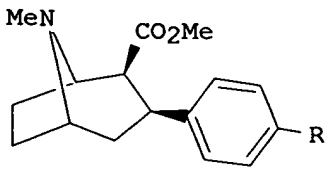


II

AB The use of dichloromethane as a solvent for the **conjugate** addition reaction of preformed ethereal solns. of phenylmagnesium bromide derivs. with anhydroecgonine Me ester (I) was found to enhance the stereoselectivity of the reaction and provide the 2β-carbomethoxy-3β-phenyltropane derivs. II (R = H, Me,Cl, F) in high yield.

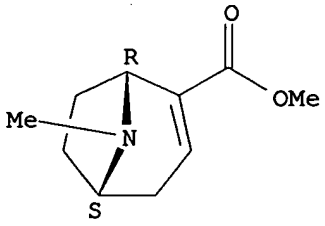
IT **43021-26-7**, (-)-Anhydroecgonine methyl ester

RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective **conjugate** addition of phenylmagnesium bromide derivs. to anhydroecgonine ester)

RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:47794 CAPLUS

DOCUMENT NUMBER: 126:131673

TITLE: Improved synthesis of β-CIT and [11C]β-CIT labeled at nitrogen or oxygen positions

AUTHOR(S): Zheng, Qi-Huang; Mulholland, G. Keith

CORPORATE SOURCE: SCHOOL MEDICINE, INDIANA UNIVERSITY, Indianapolis, IN, 46202-5121, USA

SOURCE: Nuclear Medicine and Biology (1996), 23(8), 981-986
CODEN: NMBIEO; ISSN: 0883-2897

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

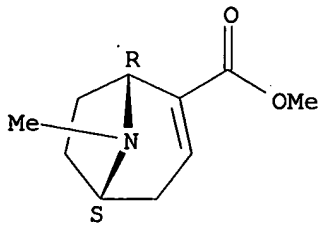
AB The important radiotracer precursor 2β-carbomethoxy-3β-(4-idophenyl)-tropane (β-CIT, RTI-55) was made in 52% overall yield from cocaine. Key steps were improved **conjugate** Grignard addition to anhydroecgonine Me ester with >3.5:1 2β: 2α-isomer selectivity, and a mild new direct aromatic iodination with I2 and silver triflate in CH2Cl2. The [11C]β-CIT was labeled at either the N or O positions with [11C]methyl triflate; and efficient reversed-phase HPLC was used to preparatively sep. [N-11C]β-CIT from N-nor-β-CIT for the first time, and a fast solid-phase extraction (SPE) method was applied to preparatively sep. [O-11C]β-CIT from β-CIT-acid precursor.

IT **43021-26-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of labeled iodophenyltropanes for use as imaging tools for neuronal monoamine uptake)

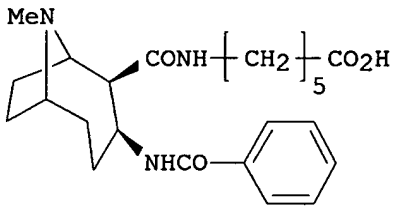
RN 43021-26-7 CAPLUS

CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L11 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:477579 CAPLUS
DOCUMENT NUMBER: 125:196066
TITLE: Design and synthesis of a cocaine-diamide **hapten** for vaccine development
AUTHOR(S): Sakurai, Mitsuya; Wirsching, Peter; Janda, Kim D.
CORPORATE SOURCE: Departments of Molecular Biology and Chemistry, The Scripps Research Institute, La Jolla, CA, 92037, USA
SOURCE: Tetrahedron Letters (1996), 37(31), 5479-5482
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



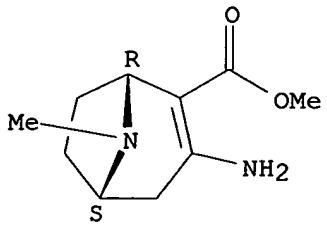
I

AB A cocaine-diamide **hapten** was designed in an effort to obtain a potent, long-lasting anti-cocaine immune response for the treatment of cocaine abuse. The analog incorporated an amido linker functionality in place of the carbomethoxy group at C-2 and a benzoylamino replacement of the benzoyloxy group at C-3 of the cocaine framework. Diamide I was synthesized in 6 steps starting from (+)-2β-carbomethoxy-3-tropinone.

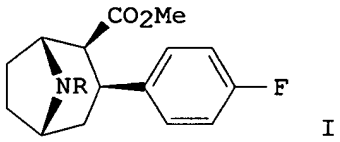
IT **180633-51-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design and synthesis of a cocaine-diamide **hapten** for vaccine development)

RN 180633-51-6 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 3-amino-8-methyl-, methyl ester, (1R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:221151 CAPLUS
DOCUMENT NUMBER: 114:221151
TITLE: Synthesis and receptor binding of N-substituted tropane derivatives. High-affinity ligands for the cocaine receptor
AUTHOR(S): Milius, Richard A.; Saha, Jayanta K.; Madras, Bertha K.; Neumeyer, John L.
CORPORATE SOURCE: Res. Biochem. Inc., Natick, MA, 01760, USA
SOURCE: Journal of Medicinal Chemistry (1991), 34(5), 1728-31
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:221151
GI

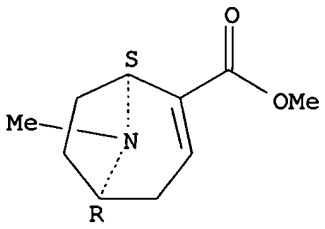


I

AB The synthesis and pharmacol. characterization of a series of N-substituted 3-(4-fluorophenyl)tropane derivs. (I; R = Me, H, CH2CH:CH2, Pr) is reported. The compds. displayed binding characteristics that paralleled those of cocaine, and several had substantially higher affinity at cocaine recognition sites. **Conjugate** addition of 4-fluorophenylmagnesium bromide to anhydroecgonine Me ester gave I (R = Me) (WIN 35,428) (II) after flash chromatog. II, the most potent analog, was tritiated at a specific activity of 81.3 Ci/mmol. The labeled compound was bound rapidly and reversibly to caudate putamen membranes; the two-component binding curve typical of cocaine analogs was observed Equilibrium was achieved within 2 h and was stable for at least 4 h. High- and low-affinity Kd values observed for [3H]-II (4.7 and 60 nM, resp.) were more than 4 times lower than those for [3H]cocaine, and the d. of binding sites [Bmax = 50 pmol/g, high, and 290 pmol/g, low) for the two drugs were comparable. Nonspecific binding of [3H]-II was 5-10% of total binding.

IT **50373-10-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with fluorophenylmagnesium bromide)
RN 50373-10-9 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, methyl ester, (1S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L11 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1923:9281 CAPLUS
DOCUMENT NUMBER: 17:9281
ORIGINAL REFERENCE NO.: 17:1643i,1644a-c
TITLE: The spectrochemistry of derivatives of tropane
AUTHOR(S): von Auwers, K.
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1922), 105, 102-19
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Extensive data are given of the optical properties of the following compds.: tropane, tropidine, tropine, acetyltropeine, propionyltropeine, tropinone, Ft tropane-2-carboxylate, Et tropidine-2-carboxylate, Me l-ecgonine, Et tropinone-2-carboxylate, tropacocaine, d-ψ-cocaine, dl ψ-cocaine, ψ-pelletierine, di-Et N-methylpyrrolidine-2,5-diacetate,2,4,6-trimethylpiperidine, N-methyl-24,6- trimethylpiperidine (prepared by boiling copellidine and MeI, diluting with H2O, filtering, making alkaline with NaOH, extracting with Et2O, drying over KOH and distilling, b. 153-5°, d4200.823). N-methyltetrahydroquinoline, bornyl acetate, isobornyl acetate, bornyl isovalerate, N-melhylcamphidine, (prepared by rubbing camphidine with MeI, diluting with a little HO2, adding NaOH, extracting with Et2O, drying over KOH and distilling, oil with an odor of camphor, b. 195-7°, slightly soluble in H2O with strong alkaline reaction, gives a precipitate with HgCl2 and H2PtCl6 (picrate, short fine needles from hot H2O, m. 234°)). The data include at various temps. d4t, nαt, ndt, nγt, Mα, MD Mβ-Mα, Mγ-Mα EMα EMD, EMβ-EMα, EMγ-EMα, EΣα, EΣD, EΣ. beta.-Σα, EΣγ-Σαand ED20. The first 8 compds. show depressions of the sp. refraction and dispersion which with slight deviations have average values of EΣrefr. = -0.5 and EΣdisp. = -9%. The next 5 compds. do not have such depressions, but only because the latter are masked by other influences, such as a **conjugate** system. The spectrochem. values of ψ/-pelletierine are similar to tropane, though structurally different. The next 5 compds. are normal, the next 3 anomalous, and the last 5 normal. Compds. containing a 7-or 8-membered ring with a =NMe group as a bridge are characterized by a spectrocbem. anomaly.

IT **137331-56-7**, Tropidine-2-carboxylic acid, ethyl ester
(optical properties of)
RN 137331-56-7 CAPLUS
CN 8-Azabicyclo[3.2.1]oct-2-ene-2-carboxylic acid, 8-methyl-, ethyl ester (9CI) (CA INDEX NAME)